AD-A185 524 MOLECULAR THEORIES OF CELL LIFE AND DEATH(U) RUTGERS - THE STATE UNIV PISCATAWAY NJ DEPT OF PHARMACOLOGY AND TOXICOLOGY S JI 27 JUL 87 AFOSR-TR-87-1186 1/1

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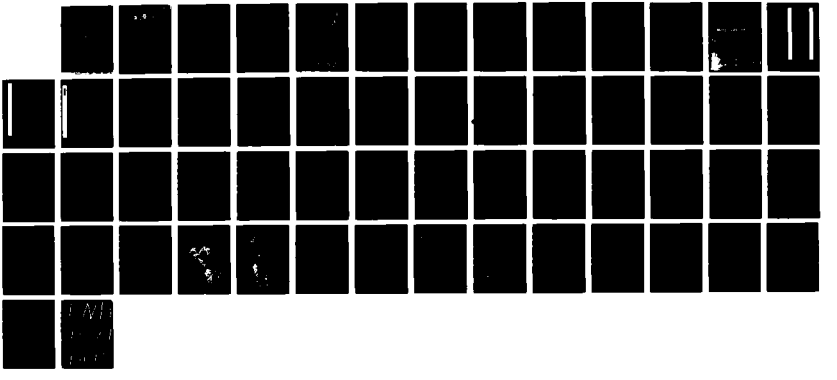

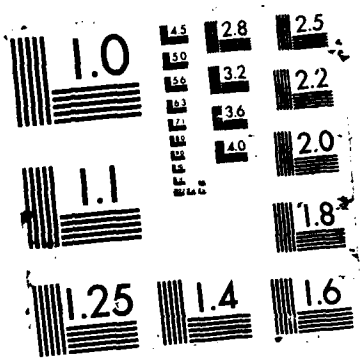
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REPORT DOCUMENTATION PAGE

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	1b. RESTRICTIVE MARKINGS
	3. DISTRIBUTION/AVAILABILITY OF REPORT Approved for public release: distribution unlimited.
4. PERFORMING ORGANIZATION REPORT NUMBER(S)	5. MONITORING ORGANIZATION REPORT NUMBER(S) AFOSR-TR- 87-1186
6a. NAME OF PERFORMING ORGANIZATION Dr. Sungchul Ji	6b. OFFICE SYMBOL (If applicable)
	7a. NAME OF MONITORING ORGANIZATION AFOSR/NL
6c. ADDRESS (City, State, and ZIP Code) Department of Pharmacology & Toxicology Rutgers University College of Pharmacy Piscataway, N.J. 08854	7b. ADDRESS (City, State, and ZIP Code) Building 410 Bolling AFB, D.C. 20332-6448
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12. PERSONAL AUTHOR(S)

Ji, Sungchul

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Final	FROM 86/03/15 TO 87/03/14	87/07/27	49

16. SUPPLEMENTARY NOTATION

The lectures given in the symposium are being assembled into a book entitled, "Molecular Theories of Cell Life and Death", to be published by early 1988. See Table of Contents.

17. COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
FIELD	GROUP	SUB-GROUP	Toxicology, molecular mechanisms of cell injury, theoretical models of cells, algebraic automata theory of biochemistry, conformons, intracellular dissipative structures

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

With the major fundings from the Air Force Office of Scientific Research Life Sciences Directorate and EPA, the first of what is being planned as a series of biennial meetings called the International Colloquium on Molecular Theories of Cell Life and Death was held on May 1 and 2, 1986 in Piscataway, New Jersey. A total of 16 speakers including two Nobel laureates (I. Prigogine and M. Eigen) delivered lectures to a group of about 100 registered attendees on topics ranging from information theory and irreversible thermodynamics to toxicology, all emphasizing their relevance to our understanding of the fundamental molecular processes underlying the phenomena of life and death of the cell. In addition to useful reviews on recent advances in experiments and theories related to the molecular biology of cells, several speakers presented new theories during the Colloquium, including the Bhopalator model of the living cell (S. Ji), the topological theory of cell death (M. Holcombe), and the "metabolic field theory" (G. Welch and H. Smith). The results of the Colloquium will be published as a book entitled Molecular Theories of Cell Life and Death and clearly indicate that there exist

(Continued on reverse)

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT	21. ABSTRACT SECURITY CLASSIFICATION
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1 AUG 1987

(Continuation from Block 19)

fundamental links between biology and physics that appear not to have been recognized heretofore. The fusion of biology and physics through these links (e.g., local gauge field theories and the mathematics of fiber bundles) may have far-reaching consequences not only for toxicology but also for life sciences and physics in general.

TABLE OF CONTENTS

FINANCIAL STATUS REPORT

(Follow instructions on the back)

1. FEDERAL AGENCY AND ORGANIZATIONAL ELEMENT TO WHICH REPORT IS SUBMITTED	2. FEDERAL GRANT OR OTHER IDENTIFYING NUMBER	OMB Approved No. 80-R0180	PAGE OF
Air Force Office of Scientific Research	AFOSR-86-0138		1 | 1 PAGES

3. RECIPIENT ORGANIZATION (Name and complete address, including ZIP code)	4. EMPLOYER IDENTIFICATION NUMBER	5. RECIPIENT ACCOUNT NUMBER OR IDENTIFYING NUMBER	6. FINAL REPORT	7. BASIS
		4-28237	☒ YES ☐ NO	☒ CASH ☐ ACCRUAL

8. PROJECT/GRANT PERIOD (See instructions)		9. PERIOD COVERED BY THIS REPORT	
FROM (Month, day, year)	TO (Month, day, year)	FROM (Month, day, year)	TO (Month, day, year)
03/15/86	03/14/87	03/15/86	03/14/87

10. PROGRAMS/FUNCTIONS/ACTIVITIES ▶	(a)	STATUS OF FUNDS (b)	(c)	(d)	(e)	(f)	TOTAL (g)
a. Net outlays previously reported	$ 0	$	$	$	$	$	$
b. Total outlays this report period	12,284						
c. *Less:* Program income credits	0						
d. Net outlays this report period (*Line b minus line c*)	12,284						
e. Net outlays to date (*Line a plus line d*)	12,284						
f. *Less:* Non-Federal share of outlays	284						
g. Total Federal share of outlays (*Line e minus line f*)	12,000						
h. Total unliquidated obligations	0						
i. *Less:* Non-Federal share of unliquidated obligations shown on line h	0						
j. Federal share of unliquidated obligations	0						
k. Total Federal share of outlays and unliquidated obligations	12,000						
l. Total cumulative amount of Federal funds authorized	12,000						
m. Unobligated balance of Federal funds	0						

20

11. RECIPIENT REFUNDS	a. TYPE OF RATE (Place "X" in appropriate box) ☐ PROVISIONAL ☐ PREDETERMINED ☐ FINAL ☐ FIXED			
	b. RATE	c. BASE	d. TOTAL AMOUNT	e. FEDERAL SHARE

12. REMARKS: Attach any explanations deemed necessary or information required by Federal sponsoring agency in compliance with governing legislation.

13. CERTIFICATION

I certify to the best of my knowledge and belief that this report is correct and complete and that all outlays and unliquidated obligations are for the purposes set forth in the award documents.

SIGNATURE OF AUTHORIZED CERTIFYING OFFICIAL

TYPED OR PRINTED NAME AND TITLE
Dr. Sunchul Ji
Associate Professor

DATE REPORT SUBMITTED
03/27/87

TELEPHONE (Area code, number and extension)
(201)932-4701

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Prescribed by Office of Management and Budget
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INSTRUCTIONS

Please type or print legibly. Items 1, 2, 3, 6, 7, 9, 10d, 10e, 10g, 10i, 10l, 11a, and 12 are self-explanatory, specific instructions for other items are as follows:

Item	Entry
4	Enter the employer identification number assigned by the U.S. Internal Revenue Service or FICE (institution) code, if required by the Federal sponsoring agency.
5	This space is reserved for an account number or other identifying numbers that may be assigned by the recipient.
8	Enter the month, day, and year of the beginning and ending of this project period. For formula grants that are not awarded on a project basis, show the grant period.
10	The purpose of vertical columns (a) through (f) is to provide financial data for each program, function, and activity in the budget as approved by the Federal sponsoring agency. If additional columns are needed, use as many additional forms as needed and indicate page number in space provided in upper right; however, the totals of all programs, functions or activities should be shown in column (g) of the first page. For agreements pertaining to several Catalog of Federal Domestic Assistance programs that do not require a further functional or activity classification breakdown, enter under columns (a) through (f) the title of the program. For grants or other assistance agreements containing multiple programs where one or more programs require a further breakdown by function or activity, use a separate form for each program showing the applicable functions or activities in the separate columns. For grants or other assistance agreements containing several functions or activities which are funded from several programs, prepare a separate form for each activity or function when requested by the Federal sponsoring agency.
10a	Enter the net outlay. This amount should be the same as the amount reported in Line 10e of the last report. If there has been an adjustment to the amount shown previously, please attach explanation. Show zero if this is the initial report.
10b	Enter the total gross program outlays (less rebates, refunds, and other discounts) for this report period, including disbursements of cash realized as program income. For reports that are prepared on a cash basis, outlays are the sum of actual cash disbursements for goods and services, the amount of indirect expense charged, the value of in-kind contributions applied, and the amount of cash advances and payments made to contractors and subgrantees. For reports prepared on an accrued expenditure basis, outlays are the sum of actual cash disbursements, the amount of indirect expense incurred, the value of in-kind contributions applied, and the net increase (or decrease) in the amounts owed by the recipient for goods and other property received and for services performed by employees, contractors, subgrantees, and other payees.
10c	Enter the amount of all program income realized in this period that is required by the terms and conditions of the Federal award to be deducted from total project costs. For reports prepared on a cash basis, enter the amount of cash income received during the reporting period. For reports prepared on an accrual basis, enter the amount of income earned since the beginning of the reporting period. When the terms or conditions allow program income to be added to the total award, explain in remarks, the source, amount and disposition of the income.
10f	Enter amount pertaining to the non-Federal share of program outlays included in the amount on line e.
10h	Enter total amount of unliquidated obligations for this project or program, including unliquidated obligations to subgrantees and contractors. Unliquidated obligations are: Cash basis—obligations incurred but not paid; Accrued expenditure basis—obligations incurred but for which an outlay has not been recorded. Do not include any amounts that have been included on lines a through g. On the final report, line h should have a zero balance.
10j	Enter the Federal share of unliquidated obligations shown on line h. The amount shown on this line should be the difference between the amounts on lines h and i.
10k	Enter the sum of the amounts shown on lines g and j. If the report is final the report should not contain any unliquidated obligations.
10m	Enter the unobligated balance of Federal funds. This amount should be the difference between lines k and l.
11b	Enter rate in effect during the reporting period.
11c	Enter amount of the base to which the rate was applied.
11d	Enter total amount of indirect cost charged during the report period.
11e	Enter amount of the Federal share charged during the report period. If more than one rate was applied during the project period, include a separate schedule showing bases against which the indirect cost rates were applied, the respective indirect rates the month, day, and year the indirect rates were in effect, amounts of indirect expense charged to the project, and the Federal share of indirect expense charged to the project to date.

U.S. Government Printing Office [illegible]

Molecular Theories of Cell Life and Death

May 1 - 2, 1986
Piscataway, New Jersey

Final Technical Report

Prepared by
Dr. Sungchul Ji
Department of Pharmacology and Toxicology
College of Pharmacy
Piscataway, New Jersey 08854

Submitted to
The Air Force Office of Scientific Research
Life Sciences Directorate

August 3, 1987

Introduction

The primary objective of the Colloquium was "to bring together internationally recognized experts from both the theoretical and experimental communities of cell-oriented researches in order to initiate dialogues among them with the ultimate goal of achieving a consensus on the definition of life and death of the cell in molecular terms." The organization of the Colloquium was motivated by the realization that, as one probes deeply into the fundamental mechanisms of cell injury and death, one is confronted with the unexpected possibility that biology and physics may be inseparably linked at the fundamental theoretical level. If this turns out to be true, biology can benefit enormously by being fused with physics, because this would allow biologists to capitalize the conceptual and theoretical frameworks established in physics to solve basic biological problems, including the cytotoxicity of chemicals and physical agents.

To this end, we invited a total of 17 speakers, out of which 16 actually participated in the Colloquium. The distribution of the specialties represented is as follows: physicists (2), chemists (1), biochemists (3), biophysicists (4), mathematicians (2), pathologist (1), and toxicologists (3). Two of the speakers were Nobel laureates in chemistry (I. Prigogine and M. Eigen), and most of the others were internationally recognized leaders in their respective fields. To attract participants to the Colloquium, about 10,000 copies of the meeting announcement (see Appendix I) were distributed through professional societies, University departments, and chemical and pharmaceutical industries throughout the North Eastern part of the U.S. Approximately 100 people registered to attend the one-and--a-half-day meeting. The final program of the meeting and the detailed description of the topics discussed are given in the pamphlet entitled "Molecular Theories" (enclosed as Appendix II).

Specific Accomplishments

1. Based on the lectures delivered at the Colloquium, we are now in the process of editing a book entitled "Molecular Theories of Cell Life and Death," most likely to be published by Academic Press in 1988 (see Appendix III for the Table of Contents). The financial support received from the Air Force Office of Scientific Research will be prominently acknowledged in the book, and a copy of the book will be forwarded to the Life Sciences Directorate when the book becomes available.
2. Many experts felt that the interdisciplinary approach characteristic of the Colloquium was very stimulating to generating new ideas and facilitated establishing new collaborations among participants. Some experts candidly admitted that they felt "vulnerable" because so many topics outside their own specialties were discussed not only during the formal lectures but also during informal gatherings throughout the Colloquium. These are the same people who usually feel very secure in more specialized meetings which they routinely attend as keynote speakers. The fact that these experts felt "vulnerable" during our Colloquium may indicate that our meeting was indeed unique and may turn out to be one of the first of a new generation of interdisciplinary meetings focused on as-yet-unexplored areas in the interface of biology and physics.
3. For the first time since its publication in 1985, the Bhopalator model of the cell was given a rare exposure to a group of distinguished scientists. The fact that there was no objection to the model raised during the Colloquium may be taken as an indication that there is no major theoretical flaws in the model.
4. Dr. M. Holcombe of the University of Sheffield has applied an algebraic

theory of machine to describe the metabolic network of the cell. Using this algebraic model of the living cell, he was able to analyze cell death in terms of topological concepts, a novel and highly original approach. His so-called "topology of cell death" promises to shed new light on the theory of cell injury and death, and his theory was formulated as a consequence of participation in our Colloquium.

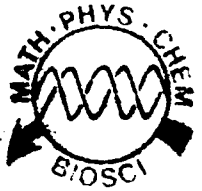
5. Another important theoretical development is the contribution by G.R. Welch and his former student H.A. Smith. They formulated what they call the "metabolic field theory" in order to discover a possible connection between the general relativity theory of Einstein and the space-time behavior of biochemical networks in the living cell. The results so far indicate that the geometric language utilized in describing general relativity may also apply to investigating the universal characteristics of cellular metabolic networks. Both the work of M. Holcombe and that of G. Welch and H. Smith increase our confidence that physics and biology may indeed be related at a deep theoretical level, a partial fulfillment of the goal of the Colloquium.

Conclusions

With the financial assistance from the Air Force Office of Scientific Research Life Sciences Directorate, we have successfully organized the first International Colloquium on Molecular Theories of Cell Life and Death in Piscataway, New Jersey from May 1 and 2, 1986. Sixteen speakers including two Nobel laureates representing the fields of mathematics, physics, chemistry, biology and medicine participated in the Colloquium which was attended by approximately 100 registered participants from the U.S. and abroad. The results of the meeting will be published in a book entitled "Molecular Theories

of Cell Life and Death," expected to be off press in 1988.

The Colloquium provided a rare opportunity for experts from traditionally uncommunicative fields (e.g., information theorists vs. toxicologists) to get acquainted and to exchange ideas and viewpoints, all relevant to the molecular biology of the living cell. Thus the cell served as a common focal point of discussions and a unifying theme. The responses from the participants of the Colloquium clearly indicate that such an interdisciplinary meeting can serve a valuable role in toxicology in particular and in biophysics in general. We are encouraged to believe that a series of 5 or 10 such meetings held biennially will go a long way toward promoting the birth of new fundamental theories in science that will unify physics and biology. The practical spin-offs from such a unification will have strong impacts in medicine and in biotechnological and biomedical industries. The conference grant awarded to us through the far-sighted leadership of the Air Force Office of Scientific Research Life Sciences Directorate has played a key role in the successful organization of what may turn out to be the first of a series of historical meetings yet to come.



International Colloquium

MOLECULAR THEORIES

Molecular Theories of Cell Life and Death — 1986

THE STATE UNIVERSITY OF NEW JERSEY
RUTGERS

Division of Continuing Education
Clifton Avenue
New Brunswick, NJ 08903

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International Colloquium

Molecular Theories of Cell Life and Death

May 1–2, 1986
Piscataway, New Jersey

Joint Graduate Program
in Toxicology
Rutgers, The State University
of New Jersey, and
University of Medicine and
Dentistry of New Jersey–
Rutgers Medical School
Piscataway, NJ 08854

Sponsors:
Rutgers, The State University
of New Jersey
University of Medicine and
Dentistry of New Jersey–
Rutgers Medical School
University of Rochester

THE STATE UNIVERSITY OF NEW JERSEY
RUTGERS

Program Description

Recent advances in experimental cell biology, biophysics, and toxicology are yielding exciting new information about the

Location

The colloquium will be held at Rutgers Medical School, Hoes Lane, Piscataway, New Jersey. A map, travel directions, and in the area will be sent with your confirmation.

10.2

University of Medicine and
Dentistry of New Jersey–
Rutgers Medical School
Piscataway, NJ 08854

Dentistry of New Jersey–
Rutgers Medical School
University of Rochester

THE STATE UNIVERSITY OF NEW JERSEY
RUTGERS

Program Description

Recent advances in experimental cell biology, biophysics, and toxicology are yielding exciting new information about the molecular principles of cell life and death. This international colloquium brings together the foremost experts in the fields of biophysics, biochemistry, toxicology, and medicine to develop a definition of cell life and death in molecular terms. The conference format is an intensive, two-day series of lectures and discussions with an international panel of scholars committed to multidisciplinary research.

Who Should Attend

The colloquium is designed for research toxicologists, biophysicists, biochemists, cell biologists, pathologists, pharmacologists, and others interested in developing cross-disciplinary molecular models of cell life and death.

Funding Sources

Financial support for the colloquium has been provided by the U.S. Environmental Protection Agency, the U.S. Air Force Life Sciences Directorate, Rutgers, The State University of New Jersey, and the University of Medicine and Dentistry of New Jersey–Rutgers Medical School.

Location

The colloquium will be held at Rutgers Medical School, Hoes Lane, Piscataway, New Jersey. A map, travel directions, and parking instructions will be sent with your registration confirmation.

A listing of area cultural and recreational activities will be provided upon your arrival. If there is sufficient interest, trips to New York City and Philadelphia will also be arranged.

Continuing Education Credits

The Office of Continuing Education of the University of Medicine and Dentistry of New Jersey designates this continuing medical education activity for 10 credit hours in Category 1 of the Physician's Recognition Award of the American Medical Association. The UMDNJ Office of Continuing Education is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians.

Hotel Accommodations

A block of rooms has been reserved at the Hyatt Regency in New Brunswick. Please make your own reservation by calling the Hyatt at 201/873-1234 or toll-free at 1-800-228-9000. Inform them that you will be attending the *Molecular Theories of Cell Life and Death* conference. A list of other lodging in the area will be sent with your confirmation.

Registration

The general registration fee of $100 provides for the two-day colloquium, two lunches, one banquet, refreshments, and educational materials. **An early bird discount fee of $90 is available for registrations postmarked by April 15.** Special discounts are available for graduate students and for faculty of Rutgers University or Rutgers Medical School.

Please complete and mail the attached registration form, or call our registrar at 201/932-7903.

Refund Policy

If you are unable to attend the program, please submit a written request for withdrawal. No refunds will be issued for withdrawals after April 30, 1986.

Tax Deduction

Educational expenses are tax deductible (registration fees, travel, meals, and lodging), if they are undertaken to improve and maintain professional skills required in one's employment or other trade or business. (Treasury Reg. 1-162-5 Coughlin vs. Commissioners 230F 2nd 307.)

International Colloquium

APPENDIX I

Molecular Theories of Cell Life and Death

May 1–2, 1986
Rutgers Medical School
Piscataway, New Jersey

Program

Thursday, May 1

9:00–9:15 A.M.
Opening Remarks
Dr. T. Alexander Pond
Executive Vice President and
Chief Academic Officer
Rutgers University

Dr. R. Reynolds
Dean
UMDNJ–Rutgers Medical School

9:15–10:00
Constructive Role of Irreversible Processes
Dr. Ilya Prigogine
(1977 Nobel Prize in Chemistry)
Free University of Brussels
Brussels, Belgium

10:00–10:30
Dissipative Structures in Biochemistry
Dr. Benno Hess
Director
Max Planck Institute for Nutrition Physiology
Dortmund, Federal Republic of Germany

10:30–11:00
Coffee Break

11:00–11:45
Quasispecies Model of RNA Replication
Dr. Manfred Eigen
(1967 Nobel Prize in Chemistry)
Max Planck Institute for Biophysical Chemistry
Göttingen, Federal Republic of Germany

11:45–12:15 P.M.
The Bhopalator—A Molecular Model of the Living Cell

2:00–2:30
Molecular Mechanisms of Cell Death
Dr. Sten Orrenius
Dean
Karolinska Institute
Stockholm, Sweden

2:30–3:00
Quantum Mechanical Models of the Living State
Dr. R.K. Mishra
Department of Biophysics
All-India-Institute of Medical Sciences
New Delhi, India

3:00–3:30
Biochemistry of Cell Death
Dr. Marion W. Anders
Department of Pharmacology
School of Medicine and Dentistry
University of Rochester
Rochester, New York

3:30–4:00
Coffee Break

4:00–4:30
Cytosociology
Dr. G. Rickey Welch
Department of Biological Sciences
University of New Orleans
New Orleans, Louisiana

4:30–5:00
Productive Cell Death
Dr. Robert L. Trelstad
Department of Pathology
Rutgers Medical School

5:00–5:30
Mathematical Models of Cell Biochemistry
Dr. Mike Holcombe
Department of Computer Science

6:00–7:00
Social Hour

7:00–8:30
Dinner

8:30–9:15
The Cytomatrix and Integration of Cell Function
Dr. Keith R. Porter
(Member, National Academy of Sciences)
Department of Biological Sciences
University of Maryland
Catonsville, Maryland

Friday, May 2

9:00–9:45 A.M.
A Mathematical Model of the Origin of Genetic Information
Dr. D.L. Stein
Department of Physics
Princeton University
Princeton, New Jersey

9:45–10:15
Role of Dissipative Structures in Immunology and Cancer
Dr. R. Lefever
Free University of Brussels
Brussels, Belgium

10:15–10:45
Coffee Break

10:45–11:15
Are Life and Death Thermodynamically or Informationally Distinguishable Alternatives?
Dr. Jerome Rothstein
Department of Computer and Information Science
Ohio State University
Columbus, Ohio

11:15–11:45
Emergent Properties, Reliability and Holistic Death in Neural Networks
Dr. Steven Finette
Department of Electrical Engineering
College of Engineering
Rutgers University

11:45–12:15 P.M.
Role of Excited States in Cell Life and Death
Dr. Helmut Sies
Director
Institute of Physiological Chemistry
University of Düsseldorf
Düsseldorf, Federal Republic of Germany

12:15–12:45
How Fundamental Knowledge Can Help Solve Practical Problems in Toxicology
Dr. Robert A. Neal
President
Chemical Industry Institute of Toxicology
Research Triangle Park, North Carolina

1:00–2:30
Lunch

2:30–4:00
Roundtable Discussion

4:00–6:00
Farewell Reception

11:00–11:45
Quasispecies Model of RNA Replication
Dr. Manfred Eigen
(1967 Nobel Prize in Chemistry)
Max Planck Institute for Biophysical Chemistry
Göttingen, Federal Republic of Germany

11:45–12:15 P.M.
The Bhopalator—A Molecular Model of the Living Cell
Dr. Sungchul Ji
Joint Graduate Program in Toxicology
College of Pharmacy
Rutgers University

12:15–2:00
Lunch

Department of Biological Sciences
University of New Orleans
New Orleans, Louisiana

4:30–5:00
Productive Cell Death
Dr. Robert L. Trelstad
Department of Pathology
Rutgers Medical School

5:00–5:30
Mathematical Models of Cell Biochemistry
Dr. Mike Holcombe
Department of Computer Science
University of Sheffield
Sheffield, England

5:30–6:00
New Alliance between Theory and Experiments in Biology
Dr. Ronald W. Estabrook
(Member, National Academy of Sciences)
Department of Biochemistry
University of Texas Health Science Center
Southwestern Medical School
Dallas, Texas

10:15–10:45
Coffee Break

10:45–11:15
Are Life and Death Thermodynamically or Informationally Distinguishable Alternatives?
Dr. Jerome Rothstein
Department of Computer and Information Science
Ohio State University
Columbus, Ohio

North Carolina

1:00–2:30
Lunch

2:30–4:00
Roundtable Discussion

4:00–6:00
Farewell Reception

For Further Information

For information regarding the scientific program, please contact Dr. Sungchul Ji, Department of Pharmacology and Toxicology, Rutgers, The State University of New Jersey, 201/932-4701. For information about the conference facilities, call Dr. Carol Goldin, Division of Continuing Education, Rutgers, The State University of New Jersey, 201/932-7999.

Registration Form

International Colloquium
Molecular Theories of Cell Life and Death
May 1–2, 1986

Name _____ Position _____

Organization _____

Address _____

City _____ State _____ ZIP Code _____

Telephone: Business _____ Home _____

☐ Early Bird Registration: $90 (if postmarked prior to April 15)

☐ General Registration: $100

☐ Rutgers University or Rutgers Medical School Faculty: $75

☐ Student: $30

Please make check payable to Rutgers University and mail to:

Ms. Leonida Eng, Registrar
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Rutgers University Graduate School - New Brunswick

Rutgers University College of Pharmacy - Office of the Dean

UMDNJ - Rutgers Medical School Department of Pathology

Joint Graduate Program in Toxicology of Rutgers University and
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INTRODUCTION

Welcome to what may turn out to be the first of a series of international meetings dedicated to the development of molecular theories of life and death on the cellular level. The need for such theories is evident to all engaged in research in any aspect of life sciences today. The explosive growth of the experimental science of living systems that we have witnessed since the discovery of the DNA double helix by Watson and Crick in 1953 both demands, and provides an exciting opportunity for, unprecedented syntheses of enormous amounts of molecular information now available into coherent, global theoretical frameworks in biology, perhaps similar to what happened in physics in the early 1900's when quantum mechanics was born and matured. It is hoped that the next several decades will bring about the emergence of general molecular theories that will account for living processes in the same way that quantum mechanics and statistical mechanics are now able to explain practically all major processes and phenomena occurring in non-living systems.

Again just as happened and is happening in physics, the successful development of a general biological theory will require a symbiotic collaboration between the experimental and theoretical communities. In analogy to the hypercycle of M. Eigen wherein two self-replicating RNA strands cooperate rather than compete with each other through the participation of enzymes they code for, experiment and theory in biology should and could cooperate with each other to achieve what may not be accomplishable by experiment or theory alone. The content of our program for the Colloquium reflects this philosophy.

Many individuals contributed to the successful organization of the Colloquium. In addition to the sponsors listed on the first page of this pamphlet, I would like to express my special thanks to Dr. Robert Snyder, director, and Dr. Bernard Goldstein, associate director of the Joint Graduate Program in Toxicology of Rutgers University and UMDNJ-Rutgers Medical School, without whose encouragement and support from the very beginning about two years ago, the Colloquium will not have taken place: to Dr. Marion Anders who first suggested holding an international symposium on cell models; to the imaginative and far-sighted leaders of both Rutgers University and UMDNJ-Rutgers Medical School for a friendly competition to sponsor the Colloquium. Finally, to Dr. Carol Goldin and her secretary, Ms. Doris Mahoney, Division of Continuing Education, Rutgers University, for ably managing the organization of the meeting.

Sungchul Ji
Chair
Organizing Committee

4/27/1986

INTERNATIONAL COLLOQUIUM ON MOLECULAR THEORIES

OF CELL LIFE AND DEATH

May 1 - 2, 1986

West Lecture Hall
Rutgers Medical School
Piscataway, New Jersey 08854

Thursday, May 1

9:00 - 9:15 a.m. (Drs. S. Ji and Robert Snyder, Chairmen)

Opening Remarks

Dr. T. A. Pond
Executive Vice President and Chief Academic Officer
Rutgers University

Dr. R. Reynolds, Dean
Rutgers Medical School
University of Medicine and Dentistry of New Jersey

9:15 - 10:00 a.m. (Dr. R. Treistad, Chairman)

Constructive Role of Irreversible Processes
Dr. Ilya Prigogine
(1977 Nobel Prize in Chemistry)
Free University of Brussels
Brussels, Belgium
and
The University of Texas
Austin, Texas

10:00 - 10:30 a.m.

Dissipative Structures in Biochemistry
Dr. Mario Markus
Max Planck Institute for Nutrition Physiology
Dortmund, Federal Republic of Germany

10:30 - 11:00 a.m.

Coffee Break

11:00 - 11:45 a.m.

Quasispecies Model of RNA Replication
Dr. Manfred Eigen
(1967 Nobel Prize in Chemistry)
Max Planck Institute for Biophysical Chemistry
Göttingen, Federal Republic of Germany

11:45 a.m. - 12:15 p.m.

The Bhopalator - A Molecular Model of the Living Cell
Dr. Sungchul Ji
Joint Graduate Program in Toxicology
College of Pharmacy
Rutgers University

12:15 - 2:00 p.m.

Lunch

2:00 - 2:30 p.m. (Dr. R. Snyder, Chairman)

Molecular Mechanisms of Cell Death
Dr. Sten Orrenius, Dean
Karolinska Institute
Stockholm, Sweden

2:30 - 3:00 p.m.

Quantum Mechanical Models of the Living State
Dr. R. K. Mishra, Vice Chancellor
North Eastern Hill University
Shillong, India

3:00 - 3:30 p.m.

Biochemistry of Cell Death
Dr. Marion W. Anders
Department of Pharmacology
School of Medicine and Dentistry
University of Rochester
Rochester, New York

3:30 - 4:00 p.m.

Coffee Break

4:00 - 4:30 p.m.

Cytosociology
Dr. G. Rickey Welch
Department of Biological Sciences
University of New Orleans
New Orleans, Louisiana

4:30 - 5:00 p.m.

Productive Cell Death
Dr. Robert L. Treistad
Department of Pathology
Rutgers Medical School

5:00 - 5:30 p.m.

Mathematical Models of Cell Biochemistry
Dr. Mike Holcombe
Department of Computer Science
University of Sheffield
Sheffield, England

5:30 - 6:00 p.m.

Solitons in DNA
Dr. Alwyn C. Scott
College of Engineering
University of Arizona
Tuscon, Arizona

6:00 - 7:00 p.m.

Social Hour

7:00 - 8:30 p.m.

Entertainment and Dinner
(Ms. Sandra West, Vocal Soloist; Mr. G. Parker, Pianist; Ms. M. Walker & Co., String Quartet, West Minster Choir College, Princeton)

8:30 - 9:15 p.m. (Dr. H. Remmer, Chairperson)

The Cytomatrix and Integration of Cell Function
Dr. Keith R. Porter
(Member, National Academy of Sciences)
Department of Biological Sciences
University of Maryland
Catonsville, Maryland

Friday, May 2, 1986

9:00 - 9:45 a.m. (Dr. M. Anders, Chairman)

A Mathematical Model of the Origin of Genetic Information
Dr. D. L. Stein
Department of Physics
Princeton University
Princeton, New Jersey

9:45 - 10:15 a.m.

Role of Dissipative Structures in Immunology and Cancer
Dr. R. Letever
Free University of Brussels
Brussels, Belgium

10:15 -10:45 a.m.

Coffee Break

10:45 - 11:15 a.m.

Are Life and Death Thermodynamically and Informationally
Distinguishable Alternatives?
Dr. Jerome Rothstein
Department of Computer and Information Science
Ohio State University
Columbus, Ohio

11:15 -11:45 a.m.

Emergent Properties, Reliability and Holistic Death in
Neural Networks
Dr. Steven Finette
Department of Electrical Engineering
College of Engineering
Rutgers University

11:45 a.m. - 12:15 p.m.

Role of Excited States in Cell Life and Death
Dr. Helmut Sies, Director
Institute of Physiological Chemistry
University of Düsseldorf
Düsseldorf, Federal Republic of Germany

12:15 - 12:45 p.m.

How Fundamental Knowledge Can Help Solve Practical Problems in Toxicology
Dr. Robert A. Neal, President
Chemical Industry Institute of Toxicology
Research Triangle Park, North Carolina

1:00 - 2:30 p.m.

Lunch

2:30 - 4:00 (Dr. B. Goldstein, Dr. M. Anders, and Dr. G. Welch)

Roundtable Discussion

Dr. I. Prigogine
"Assessment of the Colloquium from a Theoretical Physicist's Point of View"

Dr. R. Treistad
"Assessment of the Colloquium from a Biologist's Point of View"

Dr. Sungchul Ji
"Where Do We Go From Here?"

4:00 - 6:00 p.m.

Farewell Reception

KEY TERMS LIKELY TO APPEAR IN LECTURES

SPEAKER AND TOPIC	KEY WORDS AND CONCEPTS *
1. I. Prigogine Constructive Role of Irreversible processes	irreversibility energy (first law of thermodynamics) entropy (second law of thermodynamics) equilibrium structures dissipative structures near equilibrium far from equilibrium thermodynamic branch bifurcation multiple steady states non-linearity self organization spatio-temporal organization Brusselator
2. M. Markus Dissipative Structures Biochemistry	dissipative structures self organization Belousov-Zhabotinskii reaction Oregonator Brusselator glycolytic oscillations chaos simplex
3. M. Eigen Quasispecies Model of RNA Replication	hypercycle quasispecies self-replication origin of life information cooperativity self organization
4. S. Ji The Bhopalator - A Molecular Model of the Living Cell	energy entropy origin of life the Big-Bang theory information conformations of biopolymers conformational strains conformons mitochondria oxidative phosphorylation active transport

* Most of these terms are defined in the Glossary, pp. 13 - 27.

muscle contraction
Franck-Condon principle
enzymic catalysis
transition-state theory
active sites of enzymes
catalytic residues
thermal fluctuations of enzymes
binding reactions
covalent rearrangements
covalent vs. non-covalent interactions
DNA gyrase
DNA supercoils
DNA double helix
intracellular dissipative structures (IDS)
generalized gradients
redox ratios
communications
control
molecular machine
machine-environment interactions
Shannon's formula
the Bhopalator
Gibbs free energy
"Without energy, no work"
"Without information, no control"
"Without conformons, no life"

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5. S. Orrenius

Molecular Mechanisms of Cell Death

cell injury
cell death
reactive oxygen species (or metabolites)
redox cycling
intracellular Ca^{++}
intracellular Ca^{++} homeostasis hypothesis
quinones
semiquinone radicals
superoxide anion
reduced glutathione (GSH)
acetaminophen
N-acety-p-benzoquinone imine (NAPQI)
cellular protection
mixed-function oxidation
cytochromes P-450
cytoskeletons
bleb formation
LDH leakage

6.	R. K. Mishra Quantum Mechanical Models of the Living State	bosons Bose-Einstein condensation second quantization creation and annihilation operators self organization dissipative structures vivons "third quantization" (?)
7.	M. W. Anders Biochemistry of Cell Death	cell injury biological reactive intermediates carbonium ion conjugation reaction electrophiles nucleophiles covalent binding hypothesis
8.	G. R. Welch Cytosociology	multienzyme complexes cytosociology teleonomy self organization channeling of substrates enzyme catalysis zymons conformational fluctuations protein dynamics reification quasiparticles microviscosity transition state theory
9.	R. Treistad Productive Cell Death	apoptosis embryology mullerian duct collagen extracellular matrix developmental biology hydroxyproline
10.	M. Hocombe Mathematical Models of Cell Biochemistry	cellular automata theory automaton machine machine-environment interactions algebra of machines finite-state machines internal states of machines state transition probability threshold x-machine

11.	A. Scott Solitons in DNA	solitons Davydov solitons amide-I bond vibrations hydrogen bond phonons nonlinearity the nonlinear parameter (χ) self-trapping nonlinear differential equations topological solitons (kinks, antikinks) nontopological solitons polarons conformons electrets Bose-Einstein condensation "Fröhlic condensation" (?) Fröhlic theory
12.	K. Porter The Cytomatrix and Integration of Cell Function	cytoskeletons microfilaments microtubules intermediate filaments cytosol cytoplasm *cell membrane* actin myosin
13.	D. Stein A Mathematical Model of the Origin of Genetic Information	information Shannon's formula diversity stability selection frustration spin glass self organization prebiotic soup origin of life base pairing death functin evolution emergent properties mutation universality class
14.	R. Lefever Role of Dissipative Structures in Immunology and Cancer	dissipative structures self organization far from equilibrium thermoodynamic branch Brusselator

		self organizing chemical reactions immunity microcancer multiple steady states bifurcations threshold
15.	J. Rothstein Are Life and Death Thermodynamically or Informationally Distinguishable Alternatives?	information entropy generalized entropy organization structure computing measurement complexion algorithm
16.	S. Finette Emergent Properties, Reliability and Holistic Death in Neural Network	emergent properties self organization dissipative structures neural network reliability holism death computer modeling
17.	H. Sies Role of Excited States in Cell Life and Death	chemiluminescence electronic excitation free radicals reactive oxygen species singlet oxygen fluorescence lipid peroxidation organ spectrophotometry perfused organs redox state of cells in tissues photon counting
18.	R. Neal How Fundamental Knowledge Can Help Solve Practical Problems in Toxicology	toxicology chemically induced cell injury organ death organismic death cell death risk assessment environmental standards cell injury mechanisms

GLOSSARY

algebra - The branch of mathematics that uses positive and negative numbers, letters, and other systematized symbols to express and analyze the relationship between concepts of quantity in terms of formulas, equations, etc.; generalized arithmetic.

algebra of machines - The branch of algebra developed to describe the behavior of machines and their interactions with environment using algebraic expressions.

algorythm - 1) An explicit or effective procedure for producing something. 2) The act of calculating with any species of notation.

apoenzyme - The protein portion of an enzyme as contrasted with the nonprotein portion, or coenzyme, or prosthetic portion (if present).

apoptosis - Controlled cell deletion complementary to mitosis in the regulation of animal cell populations. Controlled cell death. Apoptosis = Greek, meaning "dropping off" or "falling off" of petals from flowers or leaves from trees. First coined by J.F.R. Kerr, A.H. Wyllie and A.R. Currie in 1972 (Brit. J. Cancer 26, 239 (1972)).

arithmetic - The science or art of computing by positive real numbers.

atomism - In psychology, the approach to the study of psychological phenomenon through the analysis of the elementary parts of which it is assumed to be composed in contrast to holism.

automata theory - A branch of mathematics investigating the behavior of various automata. Automata theories have been applied to modeling the development of plants and animals (A. Lindenmayer, J. Theor. Biol. 54, 3(1975)).

automaton - 1) Anything that can move or act of itself; 2) A machine or controlling mechanism designed to follow automatically a predetermined sequence of operations or respond to encoded instructions and correct errors or deviations occurring during operation.

Belousov-Zhabotinskii reaction- The oxidation of citric acid by $KBrO_3$ catalyzed by the ceric-cerous ion couple (Ce^{+4} - Ce^{+3}). This reaction has the unusual property that the progression of the reaction can lead to a temporal oscillation of the concentrations of certain chemicals participating in the reaction (e.g. Br^- and the C^{+4}/C^{+3} ratio) and a spatial pattern formation (e.g. chemical waves in a petridish or colored bands along the length of a test tube). The spatiotemporal organizations last as long as the chemical reaction proceeds. Discovered by B.B. Belousov in 1958 and later extended by A.M. Zhabotinskii (see G. Nicolis and I. Progogine. Self Organization in Non-Equilibrium systems, Wiley-InterScience Publication, New York, 1977, pp 339-353).

biological reactive intermediates - Stable chemicals that are converted into unstable, reactive intermediates catalyzed by enzymes in living tissues (e.g. the trichloromethyl radical from carbon tetrachloride catalyzed by enzymes located in the endoplasmic reticulum of the cell).

the Bhopalator - A hypothetical model of the living cell that is based on the postulate that the self-replicating properties of the cell derive from the coupling among three major classes of the cellular constituents - information-storing nucleic acids, energy-transducing enzymes, and intracellular gradients of chemical species maintained far from equilibrium through dissipation of free energy (hence called intracellular dissipative structures, IDS). The primary role of nucleic acids is to store genetic information in a stable molecular form for transmission from one gneration to another, the primary role of enzymes is to utilize the free energy released from chemical reactions to produce far-from-equilibrium distributions of matter inside the cell (i.e., IDS), and the primary role of IDS is to exchange information with, and to do work on, its extracellular environment. First proposed in Bhopal in 1983 during an international meeting (S. Ji, J. theor. Biol. 116, 399 (1985)). The Bhopalator is an example of self-organizing chemical reaction with self-replicating, self-moving, and self-thinking capabilities. In another sense, the Bhopalator can be viewed as composed of the Brusselator (i.e., IDS) and the hypercycle (i.e., the nucleic acid-enzyme cooperativity).

the Big-Bang theory - A theory in cosmology postulating that at some time about $10\text{-}15 \times 10^9$ years ago all the matter of the universe was packed into a super dense small agglomeration which was subsequently hurled in all directions at enormous speeds by a cataclysmic explosion. Also called the superdense theory.

Bose-Einstein condensation - For a vapour to the molecules of which Bose-Einstein statistics apply: the condensation of the vapour to a state in which some of the molecules have a momentum of nearly zero instead of having their momenta spread over a large range of values. This is analogous to a liquid whose molecules are in contact, instead of ranging over a large volume. The process, which was formerly regarded as hypothetical, is now believed to be related to the transition that occurs between the two forms of liquid helium at about $2{\cdot}2^{\circ}K$.

boson - Any elementary particle having integral spin (e.g., photons, mesons). Bosons obey Bose-Einstein statistics. The Pauli exclusion principle is not obeyed by bonsons. All particles are either bosons or fermions (elementary particles having half integer spin).

the Brusselator - A theoretical model of a chemical reaction proposed by Prigogine and R. Lefever in Brussels (J.Chem. Phys. 48, 1695 (1968)) that has self-organizing properties. Also called the "trimolecular model" because of the presence of a termolecular collision step in the mechanism;

$$\begin{aligned} A &\rightleftharpoons X \\ B + X &\rightleftharpoons Y + D \\ 2X + Y &\rightleftharpoons 3X \\ X &\rightleftharpoons E \end{aligned}$$

$$A + B \rightleftharpoons D + E$$

where A,B = reactants; D,E = products; X,Y = reaction intermediates.

the Ca^{++} homeostasis hypothesis - The hypothesis that, when the intracellular concentration of Ca^{++} rises beyond a certain critical level (0.1 5 x 10^{-6} M?), normal cell functions are severely perturbed, leading to cell death.

catalase - The enzyme that catalyzes the dismutation of H_2O_2 into O_2 and water.

cell water - The structure of water inside the living cell may be highly organized and not randomly mobile.

cellular automata - The mathematical systems constructed from many identical components (cells), each simple, but together capable of generating complex behavior. A one-dimensional cellular automaton consists of a line of sites, with each sites carrying a value 0 or 1 (or in general 0,.... k-1). the value oi of a site at position i is updated in discrete time steps according to an identical deterministic rule depending on a neighborhood of sites around it.

cellular protection mechanisms - Living cells have evolved to possess various mechanisms by which they can protect themselves against injurious chemical species such as reactive oxygen species and other biological reactive intermediates (e.g., GSH as a scavenger of free radicals and electrophiles)

chaos - 1) The disorder of formless matter and infinite space, supposed to have existed before the ordered universe. 2) An irregular motion which is described by deterministic equations. The essential feature of this case is that the amplitude or frequency of the process varies apparently at random (B. Hess, Hoppe-Seylers, Z. Physiol. Chem. Bd. 364,S.1 (1983)). 3) "In thermal chaos as realized in equilibrium, all characteristic space and time scales are of molecular range, while in turbulent chaos we have such an abundance of macroscopic time and length scales that the system appears chaotic." ".....in some cases the succession of bifurcations forms an irreversible evolution where the determinism of characteristic frequencies produces an increasing randomness stemming from the multiplicity of those frequencies." ".....the Feigenbaum sequence. It concerns any system whose behavior is characterized by a very general feature - that is, for a determined range of parameter values the system's behavior is periodic, with a period T; beyond this range, the period becomes 2T ("period doubling"), and beyond yet another critical threshold, the system needs 4T in order to repeat itself. The system is thus characterized by a succession of bifurcations, with successive period doubling. This constitutes a typical route going from simple periodic behavior to the complex aperiodic behavior occurring when the period has doubled ad infinitum." (I. Prigogine and I. Stengers, "Order Out of Chaos", Bantam Books, Toronto, 1984, p. 168).

chemical oscillations - Under appropriate conditions, the concentrations of certain chemical species participating in self-organizing chemical reactions can oscillate in time (e.g., the Br^- concentration in the Belousov-Zhabotinskii reaction).

chemical potential - The change in the free energy of the system with a change in the chemical composition due to chemical reaction or due to matter transport. Under the condition of constant temperature, any change in the system proceeds from a state of higher chemical potential to a state of lower chemical potential. At constant temperature and pressure, the chemical potential is given by Gibbs free energy (G); and under constant temperature and varying pressure, the chemical potential of the system is given by Helmholtz free energy (H).

chemical waves - During certain self-organizing chemical reactions proceeding under appropriate conditions, the concentrations of some chemicals can vary in space, forming wave-like or spiral-like patterns.

chemiluminescence - The emission of photons from energy-releasing chemical reactions.

chromatin - The genetic material of the nucleus consisting of deoxyribonucleoprotein. During mitotic division the chromatin condenses to form chromosomes.

chromosome - One of the bodies (normally 46 in man) in the cell nucleus that is the bearer of genes.

coenzymes - Substances that are necessary for the catalytic action of enzymes. Coenzymes are of smaller molecular size than the enzymes themselves (e.g. several vitamins such as thiamine, pyridoxal, nicotinamide).

cofactor - A prosthetic group such as heme, coenzymes, and inorganic ions such as magnesium ion, essential for enzyme action

configuration - Unlike conformation, the configuration of a molecule cannot be changed without breaking at least one covalent bond.

conformons - Mobile energy packets stored in the form of conformational strains of biopolymers (nucleic acids and enzymes). Conformons carry potential energy (due to strains) and information (in the form of the unique spatiotemporal alignments of catalytic amino acid residues in enzymic active sites or nucleotide bases in functional sites of nucleic acids). Because of the availability of both energy (to do work) and information (to control work), conformons can drive controlled molecular work processes in enzymes and nucleic acids, leading to goal-oriented catalysis, molecular recognition, and gene expression (S. Ji., Ann. N.Y. Acad. Sci. 227, 211-226 and 419-437 (1974); Asian J. Exp. Sci. 1, 1 (1985); J. theor. Biol. 116, 399 (1985)). There is a great similarity between conformons and "frustrations" in spin glass. The latter concept was recently employed by P.W. Anderson to develop a model of origin of life (Proc. Nat. Acad. Sci. 80, 3386 (1986); Ibid 81, 1751 (1984)).

conjugation reactions - Cells remove foreign compounds (xenobiotics) by sulfation or glucuronidation, or by adding the glutathionyl group. These reactions are called conjugation reactions, or phase II reactions.

control - Synonymous with regulation. Influencing a device or machine in such a way as to achieve a specific goal.

the covalent binding hypothesis - Many chemicals injure cells by being converted into biological reactive intermediates (BRI) which subsequently bind covalently to essential cellular macromolecules like enzymes, phospholipids, and nucleic acids. Formulated in the early 1970's by Mitchell, Jollow, Gillette, Potter, Davis and Brodie.

creation and annihilation operators - A creation operator, a_l^+, is defined in such a way that, when acting on a basis vector, adds a particle to it with quantum number l. Similarly, an annihilation operator, a_l, will remove a particle with quantum number l upon acting on a basis vector.

cytochromes P-450 - A group of enzymes that have a heme and an iron ion at the active site and absorb maximally at 450 nm when reduced in the presence of carbon monoxide. These enzymes participate in mono-oxygenation reactions of various chemicals, both endogenous and exogenous. Discovered in the early 1960's by Omura and Sato.

cytoskeletons - A group of filamentous protein molecules (microfilaments; microtubules) that provide highly organized structures to the cytoplasm of the living cell. Also called the cytomatrix.

cytosociology - The concept that the various enzymes in the living cell are not randomly distributed but form a coherently interacting organized system in the cytoplasm. (R. Welch and T. Keleti, J. theor. Biol. 93, 701 (1981)).

dissipative structures - Any distribution of matter in space and in time that is maintained far from equilibrium through dissipation of free energy (e.g., the flame of a candle; the K^+ and Na^+ ion gradients across the cell membrane; self-organizing chemical reactions such as the Belousov-Zhabotinskii reaction).

DNA gyrase - A bacterial enzyme that uses the energy of ATP hydrolysis to pump supercoils continuously into the DNA, thereby maintaining conformational strains in localized regions called looped domains (B. Alberts et al. The Cell, Garland Publishing Inc., New York, 1983, p. 446).

DNA supercoils - The helical turns of a double-stranded DNA molecule generated when the DNA double helix is rotated around the helical axis. The potential energy stored in one supercoil is sufficient to break the hydrogen bonds of 10 base pairs.

electric potential - Symbol: V. The electric potential at a point in an electric field is the work required to bring unit positive electric charge from infinity to the point. It is measured in volts. If work of 1 joule is required to move a charge of 1 coulomb to the point its potential is 1 volt.

electrophiles - Any chemical species having a great tendency to react with a electron-rich center (e.g., carbonium ions, electron-deficient carbon centers such as the carbonyl carbon).

emergent property - A property of a complex system which is not contained in its parts (e.g., rigidity, superconductivity, conciousness).

endergonic - Free-energy consuming (e.g., muscle contraction, active transport).

energy - The property of a system that is a measure of its capacity for doing work. The energy of an isolated system (e.g., the Universe) remains constant (the First Law of thermodynamics). Energy and mass are interconvertible according to Einstein's law. $E = mC^2$.

entropy - The thermodynamic function of a system that is a measure of the degradation of the system (e.g., when a crystal dissolves in water to form a solution; when the human body decays due to starvation). A measure of randomness or uncertainty. Whenever irreversible processes occur, the entropy of the universe must increase (the Second Law of Thermodynamics). In addition to the "thermodynamic" entropy defined above, the term "information theoretic" entropy is frequently used. The latter is equivalent to the information defined by Shannon's formula (see information). The information theoretic entropy of a message can be regarded as a measure of the uncertainty that is removed as a consequence of receiving the information.

enzymes - Protein molecules that can accelerate the rate of chemical reactions which proceed very slowly or not at all in their absence. Most, if not all, chemical reactions occurring in the living cell are enzyme-catalyzed.

enthalpy - A therodynamic function (i.e., the value of the function depends only on the initial and final states of the system and independent on the path followed) defined as E + PV, where E is the internal energy ot a system, P the pressure and V the volume.

equilibrium structures - Distributions of matter in space that persist without the need of dissipating free energy (e.g., crystals, lipid bilayers, etc).

excited state - When a molecule absorbs energy, it can be excited to a higher energy state through electronic, vibrational, or rotational excitations.

exergonic - Free-energy releasing (e.g., $ATP + H_2O \rightarrow ADP + P_i + H^+$).

extracellular matrix - Proteins and other materials that form a deformable structural matrix outside the cell.

Franck-Condon principle - 1) The absorption of visible or ultraviolet light by a molecule occurs by a process which substitutes a new electronic structure for an old electronic structure so rapidly that there is no significant change in internuclear distance during the course of the transition. This is due to the fact that electrons have velocities about 100 times (or more) greater than that of vibrating nuclei (typically 10^8 cm/sec vs. 10^6 cm/sec). First proposed by J. Franck in 1925 (Trans. Faraday Soc. 21,536 (1925)) and later put on a theoretical basis by E.U. Condon in 1928 (Phys. Rev. 32,858 (1928)) in order to account for the electronic and vibrational spectral data of simple molecules. 2) W.F. Libby (J. Phys. Chem. 56,863 (1952)) extended the Franck-Condon principle to include inorganic electron transfer reactions with the conclusion that inorganic electron transfer processes in aqueous media (e.g. from Fe^{+2} to Fe^{+3}) must be preceded by the reorganization of the primary hydration shells around the electron donor (Fe^{+2}) and acceptor (Fe^{+3}). 3) In 1974, the Franck-Condon principle was applied for the first time to the molecular mechanism of enzymic catalysis (S. Ji, Ann. N.Y. Acad. Sci. 227,432 (1974)). According to the so-called generalized Franck-Condon principle, the rate of the electronic rearrangement of a substrate bound to an active site of an enzyme (i.e., catalysis) is determined by the rate with which the catalytic residues of that active site can rearrange to a conformational state complementary to the altered substrate structure which is intermediate between the molecular shape of the bound reactant and that of the bound product. Since it is reasonable to think that the rate of conformational rearrangements of an enzyme would depend on the amino acid sequence of the protein, it follows that the rate of enzymic catalysis can be encoded in the primary sequence of an enzyme. Therefore, the enzymic theory based on the Franck-Condon principle provides a possible molecular mechanism to link the genetic information of DNA to specific rate constants of elementary chemical reaction steps catalyzed by an enzyme. The strained conformational state of the catalytic residues that is localized at the active site and precedes an electronic rearrangement of a bound substrate is named the Franck-Condon conformon (S. Ji, J. Theor. Biol. 116,399 (1985)).

the Fenton Reaction - The electron transfer reaction from reduced Fe^{+2} or Cu^{+} to H_2O_2 to generate HO·; $H_2O_2 + Fe^{+2}$ (or Cu^{+}) $\longrightarrow$ $HO^{\cdot} + HO^{-} + Fe^{+3}$ (or Cu^{+2}).

fermion - Any elementary particles having halt interger spin (e.g., electrons). Fermions obey Fermi-Dirac statistics. The Pauli exclusion principle is obeyed by fermions.

fluctuations - Random thermal motions of molecules and intramolecular segments of polymers.

free energy - A thermodynamic function (a function of a system that depends only upon the initial and final states of the system and is independent of the path followed) that gives the amount of work available when a system undergoes some specified change.

free radicals - Reactive chemical species that possess an unpaired (or odd) electron (e.g., $\cdot CCl_3$, $O_2^{\pm}$ etc.). Free radicals can be divided into anion free radicals (odd electron + negative charge), cation free radicals (odd electron + positive charge), and neutral free radical (odd electron with no electrical charge).

frustrations - When a system consists of numerous interacting componets (e.g., electron spins in spin glass), it is often impossible to arrange all the components in such a way that all of them exist in the minimum energy states. For example, if one considers a system of three electrons in glassy solid state in which each electron can exist with its spin directed either up (u) or down (d); and if one further assumes that the antiparallel spin arrangements (du or ud) is of a lower energy content than the parallel arrangement (uu or dd), then there are two possible arrangements of 3 electrons, namely duu and udd, that contain one unfavorable interaction between neighboring electrons that cannot be avoided no matter how one arranges the middle electron. This is an example of frustration. Conformational strains of biopolymers can be regarded as equivalent to frustrations in spin glass.

gene - The functional unit of heredity. Each gene occupies a specific place or locus on a chromosome, is capable of reproducing itself exactly, at each cell division, and is capable of directing the formation of an enzyme or other proteins.

generalized "membrane potential" - 1) The rate of change of the intracellular concentration of a chemical species with respect to the space coordinates (x, y, z) or time coordinate (t): $dC/dQ \neq 0$ where C = the concentration (or activity) of an intracellular chemical species, and Q = the generalized coordinate whose components are x, y, z and t. 2) The inhomogeneous distribution of matter inside the living cell with respect to space or time or both. 3) Any nonequilibrium distribution of matter inside the cell (e.g., $[K^+]$in, $[Na^+]$in, $[Ca^{++}]$in, NADH/NAD^+, $[H^+]$mito/$[H^+]$cytosol, etc.). 4) Synonymous with the intracellular dissipative structure (IDS).

Gibbs free energy - Defined by the relation,

$$G = E + PV - TS$$

where G = Gibbs free energy, E = internal energy, P = pressure, V = volume, T = temperature, and S = entropy. The Gibbs free energy of a system approaches zero as the system becomes equilibrated under constant T and P.

glutathione peroxidase - The enzyme that catalyzes the oxidation of reduced glutathione (GSH) by H_2O_2; $2GSH + H_2O_2 \longrightarrow GSSG + 2H_2O$.

gnergy - A new term formed from the Greek roots, "gne-" (to know) and "-ergy" (to work), to indicate a physical entity composed of energy (to do work) and information (to control work) thought to be essential for performing goal-oriented or goal-seeking work processes (S. Ji, J. Theor. Biol. 116,399 (1985)). The fundamental units of gnergy may be called "gnergons". The gnergons essential for driving the goal-oriented behaviors of biopolymers in the living cell (e.g., enzymic catalysis, active transport, contraction of the actomyosin system, etc.) are identified with conformons (conformational strains of biopolymers carrying free energy and genetic information), and the gnergons essential for the living cell to communicate with its environment (e.g., chemotaxis, mitosis, secretion of hormones, etc.) are identified with intracellular dissipative structures (IDS).

gradient - The gradient of a scalar field f(x,y,z) at a point is the vector pointing in the direction of the greatest increase in the scalar with distance (i.e. perpendicular to the level surface at the point in question). It has components along the coordinate axes that are the partial derivatives, f_x, f_y, f_z of the function with respect to each variable: grad $f = \nabla f = If_x + Jf_y + Kf_z$, where ∇ is the differential operator and I, J and K are unit vectors along the x-, y-, and z-axis.

the Harber-Weiss reaction - The electron transfer reaction from $O_2^{\cdot}$ to H_2O_2 to generate HO·; $O_2^{\cdot} + H_2O_2 \longrightarrow O_2 + HO\cdot + HO^-$. This reaction is catalyzed by Cu and Fe.

holism - In psychology, the approach to the study of a psychological phenomenon through te analysis of the phenomenon as a complete entity in itself. In contrast to atomism.

holoenzyme - The complete enzyme, i.e., apoenzyme + coenzyme.

hypercycle - A system of RNA strands and conjugate enzymes that are mutually coupled in such a way that a cooperation, rather than competition, results among self-replicating RNA strands. For example, an information-carrying RNA (I_1) codes for a primitive enzyme (E_1) that helps replicate another RNA (I_2), which similarly helps to replicate I_1 through its translation product (E_2). Therefore, the sequence of information transfer is: $I_1 \rightarrow E_1 \rightarrow I_2 \rightarrow E_2 \rightarrow I_1$, etc. The hypercycle of M. Eigen and P. Schuster (The Hypercycle: Springer-Verlag, Berlin, 1979) can be regarded as an example of self-organizing chemical reactions catalyzed cooperatively by RNA strands and enzymes that lead to a self-replication.

information - "A measure of one's freedom of choice when one selects a message" (W. Weaver, in The Mathematical Theory of Communication by C.E. Shannon and W. Weaver, University of Illinois Press, Urbana, 1949, p.9). The smallest amount of information is 1 bit (binary digit) which is equivalent to the amount of information required to correctly predict the outcome of one toss of a coin. In general, the amount of the information carried by a message can be calculated by using Shannon's formula:

$$I = \log_2 \frac{Wo}{W}$$

Where I = the amount of information expressed in bits, Wo = the total number of possible messages (e.g., all possible DNA molecules 10^9 nucleotride long), W = the number of messages actually selected (e.g., all possible 10^9 nucleotide - long DNA molecules that carry genetic information). When W = 1, I is maximal. The above equation holds only when the probabilities of chosing different messages are equal. There is another aspect to information; i.e., the meaning or the semantics of information (see M.V. Volkenstein, Foundations of Physics 7:97 (1984)) which is independent of the amount of information (e.g., of the immense number of 10^9 nucleotide-long DNA molecules, only a very small fraction will carry biologically meaningful genetic information).

Irreversible change - Changes in which the system is not in equilibrium at all instants during the change. All practical processes involve irreversible changes. Associated with all irreversible changes is a net production of entropy.

kinetic energy - The energy possessed by virtue of motion, equal to the work that would be required to bring the body to rest.

limit cycle - 1) Special solutions of differential equations that can be represented by closed curves in the phase plane (N. Minorsky, Non-Linear Oscillations, R.E. Krieger Publ. Co., Huntington, N.Y., 1974). 2) If one plots the concentrations of the substrate and the product of an oscillating chemical reaction on the x- and y-axes, respectively (i.e. forms a "phase plane"), the time evolution of the reaction system tends toward a closed loop or circle in the phase plane. This stable trajectory is called the "limit cycle", term first used by H. Poincare' in 1881.

lipid peroxidation - The oxidation of lipids leading to the formation of peroxides, namely compounds containing the peroxy group, -O-O-.

looped domains - Segments of DNA double helix forming a loop, 10^2 - 10^3 nucleotide long.

machine - A device for doing work. In a macroscopic machine, a comparatively small force called the "effort" is used to overcome a large force (e.g. the weight lifted by a system of pulleys) called the "load". The ratio, load/effort, is the "mechanical advantage" or "force ratio".

membrane potential - The electrical potential difference that exists between the cytoplasm and the extracellular medium of the living cell. Always smaller than 100 mV. The membrane potential is generated as a result of the balance between the active transport of ions across biomembranes catalyzed by energy-driven pumps located in the membrane and the passive diffusion of ions through channels spanning the membrane.

mitochondrion - The subcellular organelle responsible for coupling the oxidation of substrates to the synthesis of ATP (oxidative phosphorylation), the universal currency of free energy in the cell. Thousands of mitochondria are contained in each cell.

mitosis - The usual process of cell reproduction consisting of a sequence of modifications of the nucleus (prophase, prometaphase, metaphase, anaphase, Telophase) that result in the formation of two daughter cells with exactly the same chromosome and DNA content as that of the original cell.

molecular machine - A biopolymer or a system of biopolymers (e.g. enzymes, DNA, RNA) that can utilize chemical or light energy to perform work on its environment, including transport of mass in space (e.g. active transport, muscle contraction, chromatin structural rearrangement, biosynthesis). Unlike macroscopic machines, a molecular (or microscopic) machine must be able to undergo thermal fluctuations (i.e., conformationally dynamic) so that it can receive energy from an external source, store the energy as conformational strains for times longer than characteristic times of thermal motions, and utilize it to perform catalysis or mechanical work.

multienzyme complexes - Systems of enzymes organized to maximize the catalytic efficency of component enzymes. For example, substrates and products involved in catalyses may be channeled between appropriate enzymes and not allowed to freely diffuse away into the cytosol before catalyses are completed.

non-linearity - 1) Differential equations containing terms other than the differential terms raised to the 1st power. 2) Any observables whose magnitude is a non-linear function of independent variables (e.g., enzymic rate is a non-linear function of substrate concentrations in Michaelis-Menten kinetics).

nucleophiles - Any chemical species that have a great tendency to react with an electron-deficient center (and hence exposed nucleus of an atom) (e.g., carbanion, HO^-, O_2^-).

neural network - A system of structural and functional interconnections among neurons.

organization - Whenever a particular pattern of distribution of matter in space and/or time is selected out of a group of alternative choices, the selected distribution of matter is said to possess an increased amount of information as defined by Shannon's formula and a higher degree of organization. In this sense, the terms organization, structure, and information can be treated as equivalent (see J. Rothstein, in The Maximum Entropy Formalism, ed. by R.D. Levine and M. Tribus, The MIT Press, Cambridge, 1979, pp. 423-468).

the Oregonator - A kinetic model of the self-organizing Belousov-Zhabotinskii reaction proposed by J. Field and R. M. Noyes in Oregon (J. Chem. Phys. 60, 1877 (1974)).

origin of life - Many believe that the first self-replicating molecular system (e.g., self-replicating RNA strands) originated on the surface of the earth spontaneously about 2-3 billion years ago. The first Homo sapiens is believed to have originated from ape-like creatures about 300,000 years ago. The universe began about 15 billion years ago.

phase I and II reactions - Cells have the capacity to remove hydrophobic xenobiotics by first hydroxylating them through the cytochrome P-450-mediated mono-oxygenation reaction (phase I reaction) and then adding polar groups through glucuronidation or sulfation (phase II reactions).

phase space - A multidimensional space in which the coordinates represent the variables required to specify the state of the system. In particular, a six-dimensional space incorporating three dimensions of positon and three of momentum.

photon - The quantum of electromagnetic radiation.

potential - Electrostatic, magnetostatic, and gravitational potentials, at a point in the field: the work done in bringing unit positive charge, unit positive pole, or unit mass respectively from infinity (i.e. a place infinitely distant from the causes of the field) to the point.

potential energy - The energy possessed by a body or system by virtue of position, equal to the work done in changing the system from some standard configuration to this existing state.

potential gradient - The rate of change of potential, V, at a point with respect to distance x, measured in the direction in which the variation is a maximum. It is measured in volts per meter (e.g. the membrane potential of normal cells = 60 mv/60A = 10^5 V/cm). The electric field strength, E, is numerically equal to the potential gradient but in the opposite sense: $E = - dV/dx$.

prostaglandins (PG) - A group of lipid-soluble compounds first isolated from the prostate gland in 1935 by U.S. von Euler. PG's have a wide variety of pharmacological effects on living tissues and are all derived from the 20-carbon fatty acid, arachidonic acid, released from biomembranes by the action of phospholipases.

protein dynamics - Enzymes under physiological conditions are constantly undergoing rapid fluctuating motions. Such fluctuations are thought by many to be essential for initiating catalysis.

quantum - The smallest, discrete unit of energy in nature. First invoked by M. Planck in 1900 in order to explain the phenomenon of the "ultraviolet catastrophe" in black-body radiation. Planck postulated that an oscillator could acquire energy only in discrete units called quanta. In 1905, Einstein employed the concept of quanta to explain the photoelectric effect by assuming that light was radiated in quanta (photons).

quantum field theory - A field theory in which all the physical observables of a system are represented by appropriate operators which obey certain commutation relations. The quantized field can be considered as an assembly of particles each of which is characterized by its own energy, momentum, charge, etc., the total energy, momentrum, etc., of the field being built up additively from the individual contributions of the particles present. Any particle may thus be considered as a "quantum" of a corresponding field.

reactive oxygen species - The oxygen molecule, O_2, can be reduced by adding 1, 2, 3 or 4 electrons to generate $O_2^{\cdot-}$ (superoxide anion), H_2O_2 (hydrogen peroxide), HO• (hydroxyl radical) + HO^- (hydroxide anion), or $2HO^-$, respectively. Of these, $O_2^{\cdot-}$, H_2O_2 and HO• are chemically reactive and hence are called reactive oxygen species or reactive oxygen metabolites. In addition, the electronically excited oxygen molecule called the "singlet" oxygen that can be generated under appropriate conditions is also included as a member of reactive oxygen species.

receptors - Protein molecules that posses a high affinity for a select molecule (or ligand) and exclude others. Receptors can be located in biomembranes or in the cytosol or the nucleus. Receptors can be distinguished from enzymes because receptors in general do not catalyze chemical reactions.

redox cycling - The cyclical reduction and oxidation reaction catalyzed by certain chemicals which have the ability to receive one electron to form a metastable anion radical which in turn donates one electron to an acceptor (e.g., O_2) to regenerate the original molecule. Quinones are well known examples of redox cyclers.

reification - 1) To treat an abstraction as substantially existing, or as a concrete material object; 2) The conversion of virtual particles of vacuum into real particles through input of energy.

relativistic quantum theory - The quantum theory of particles which is consistent with the special theory of relativity, and thus can describe particles moving arbitrarily close to the speed of light.

reversible change - A change that is carried in such a way that the system is in equilibrium at any instant and that a slight decrease in the factor affecting the change causes every feature of the forward process to be completely reversed.

second quantization - Quantization of fields. Introduced to describe many-body identical particle systems. It is the process by which a classical field may be considered as an assembly of particles. Wave functions in the traditional quantum mechanics derived from the first quantization are replaced by field operators, and these and all other physical operators act on the Fock space, whose basis vectors consist of occupation numbers of various quantum states.

simplex - The simplest polyhedron in a given geometric space. The simplex of the 2-dimensional space is a triangle; the simplex of the 3-dimensional space is a tetrahedron. In general, the n-dimensional simplex has (n+1) vertices.

solitons - 1) The term was coined in 1965 by N.J. Zabusky and M.D. Kruskal (Phys. Rev. Lett. 15,240 (1965)) to indicate a special solution to a non-linear differential equation which was developed in 1885 by Kortweg and de Vries to describe the solitary wave phenomenon (i.e., solitary water waves that travel long distances without dispersion) first observed by J.S. Russel in 1844. This mathematical equation is known as the Kortweg-de Vries equation. 2) The generic term denoting all examples of dynamic, localized structural deformations (e.g. water waves, protein conformational strains, etc.) that carry energy (A.C. Scott, Comments Mol. Cell. Biophys. 3(1),15 (1985)). 3) Conformons (conformational strains of biopolymers selected by evolution to perform biological functions) can be regarded as solitons of biopolymers endowed with some useful biological functions. Conformons are solitons, but not all solitons of biopolymers are conformons (S. Ji, in The Living State - II (R.K. Mishra, ed.), World Scientific Publishing Co., Singapore, 1985, pp. 565-574).

spatiotemporal organization - Organization of matter both in space and in time (e.g., Belousov-Zhabotinskii reactions; development of embryos).

superoxide dismutase (SOD) - The enzyme that catalyzes the dismutation of superoxide anion into hydrogen peroxide and oxygen.

$$2O_2^{\cdot-} \longrightarrow H_2O_2 + O_2$$

Discovered by J. M. McCord and I. Fridovich in 1969.

symbiosis - Any intimate association between two species.

symmetry - 1) Equality or correspondence in form of parts distributed around a center or an axis, at the two extremities or poles, or on the two opposite sides of any body. 2) Any property of an object, material or mathematical, that remains constant upon changing the object in certain ways.

symmetry breaking - A process by which the degree of the symmetry of an object or entity is reduced (e.g., thermal gradient-driven convective flow of a fluid, ATP-driven active transport of cations across biomembranes).

teleonomy - The doctrine that life is characterized by endowment with a project or purpose; i.e., the existence in an organism of a structure or function implies that it has had evolutionary survival value.

thermal energy - The energy associated with a system of molecules or atoms undergoing vibrational, rotational or translational motions at a given temperature. Thermal energies can be harnessed to perform useful work only during a heat flow along a temperature gradient.

topology - A branch of mathematics that deals with the properties of a geometric figure which do not vary when the figure is transformed in certain ways.

toxicology - 1) The science of poisons - their source, chemical composition, action, tests, and antidotes. 2) The science aimed at elucidating molecular mechanisms of interactions between chemicals and living sytems (cells, organs, organisms, and societies) that lead to undesirable effects on human health.

useful numbers - 1) h (Planck's constant) = 6.626×10^{-27} erg·sec
$= 1.58 \times 10^{-34}$ cal·sec
2) 1 eV = 23 kcal/mole
3) N (Avogadro's number) = 6×10^{23}
4) 1 cm^{-1} = 2.85 cal/mole
5) ΔG_{ATP} (free energy of hydrolysis of ATP) = 16 kcal/mole.
6) the vibrational quantum of the amide-I bond (i.e. the stretching motion of the C = O bond) = 1660 cm^{-1}
= 4.73 kcal/mole (or einstein).

virtual particles - Because of the uncertainty principle it is possible for the law of conservation of mass and energy to be broken by an amount ΔE providing this only occurs for a time Δt such that $\Delta E \cdot \Delta t \leq h/4\pi$, where h = Planck constant, 6.63×10^{-27} ergs. sec. This makes it possible for particles to be created for short periods of time where their creation would normally violate conservation of energy. These particles are called virtual particles. The electrostatic force between charged particles may be described in terms of the emission and absorption of virtual photons by the particles.

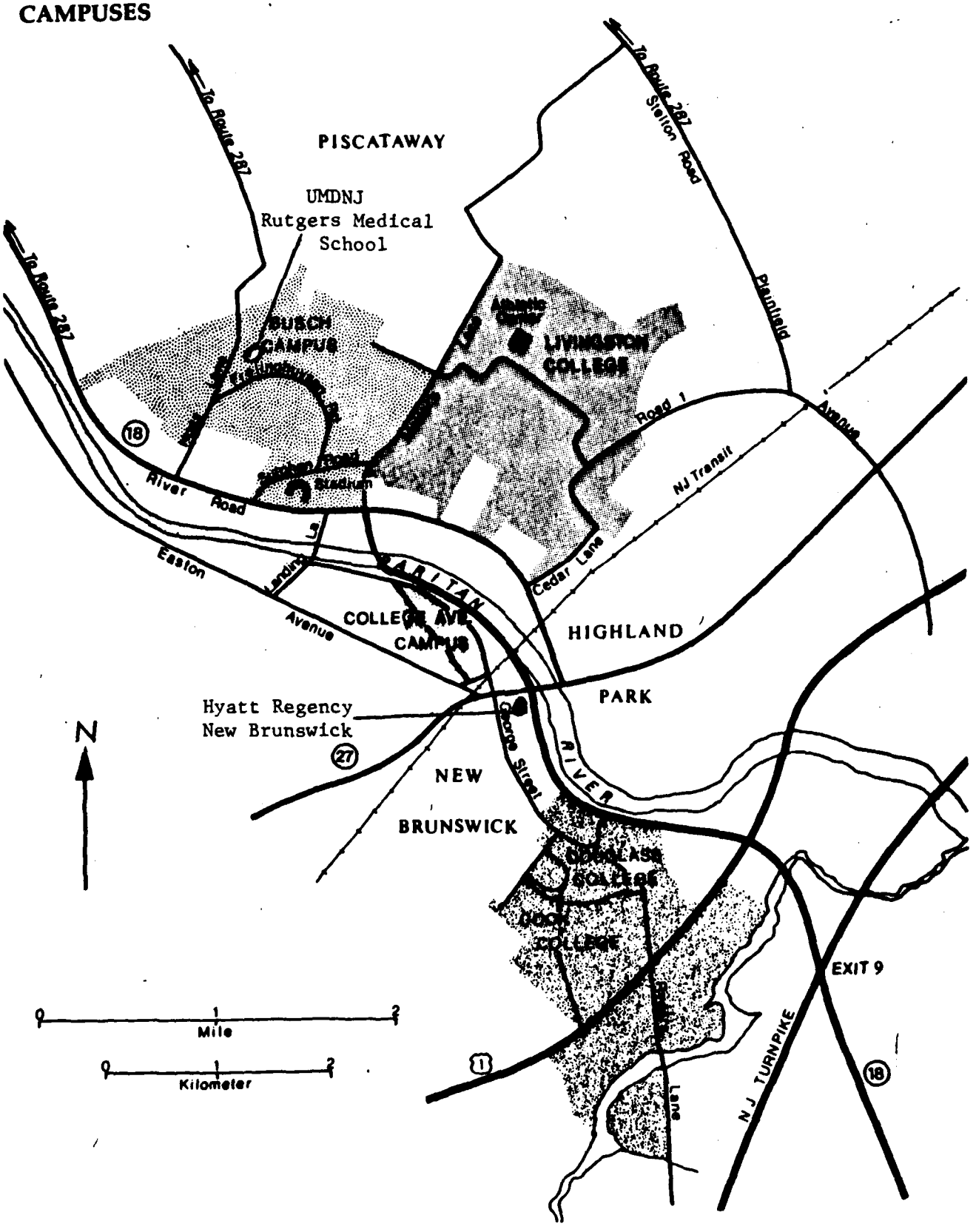
wave function - Symbol: ψ. A mathematical function appearing in the Schrödinger wave equation and describing the behavior of a particle according to wave mechanics. The particle is thought of as a wave and ψ is the displacement or amplitude of this wave with respect to position. The square of the amplitude of the matter wave, $|\psi|^2$ is proportional to the probability of finding the particle in a specified position.

wave number - Symbol ν. The number of waves per unit path length (units = cm^{-1}, m^{-1}, etc.). The reciprocal of the wavelength.

zymons - Quasi-particles representing transient correlated motions of groups of particles in enzymes. Thought to be involved in the energization of enzyme active sites (B. Somogyi, G. R. Welch and S. Damjanovich, Biochim. Biophys. Acta. 768, 81(1984)). Similar to or identical with conformons.

RUTGERS, THE STATE UNIVERSITY

NEW BRUNSWICK/PISCATAWAY CAMPUSES



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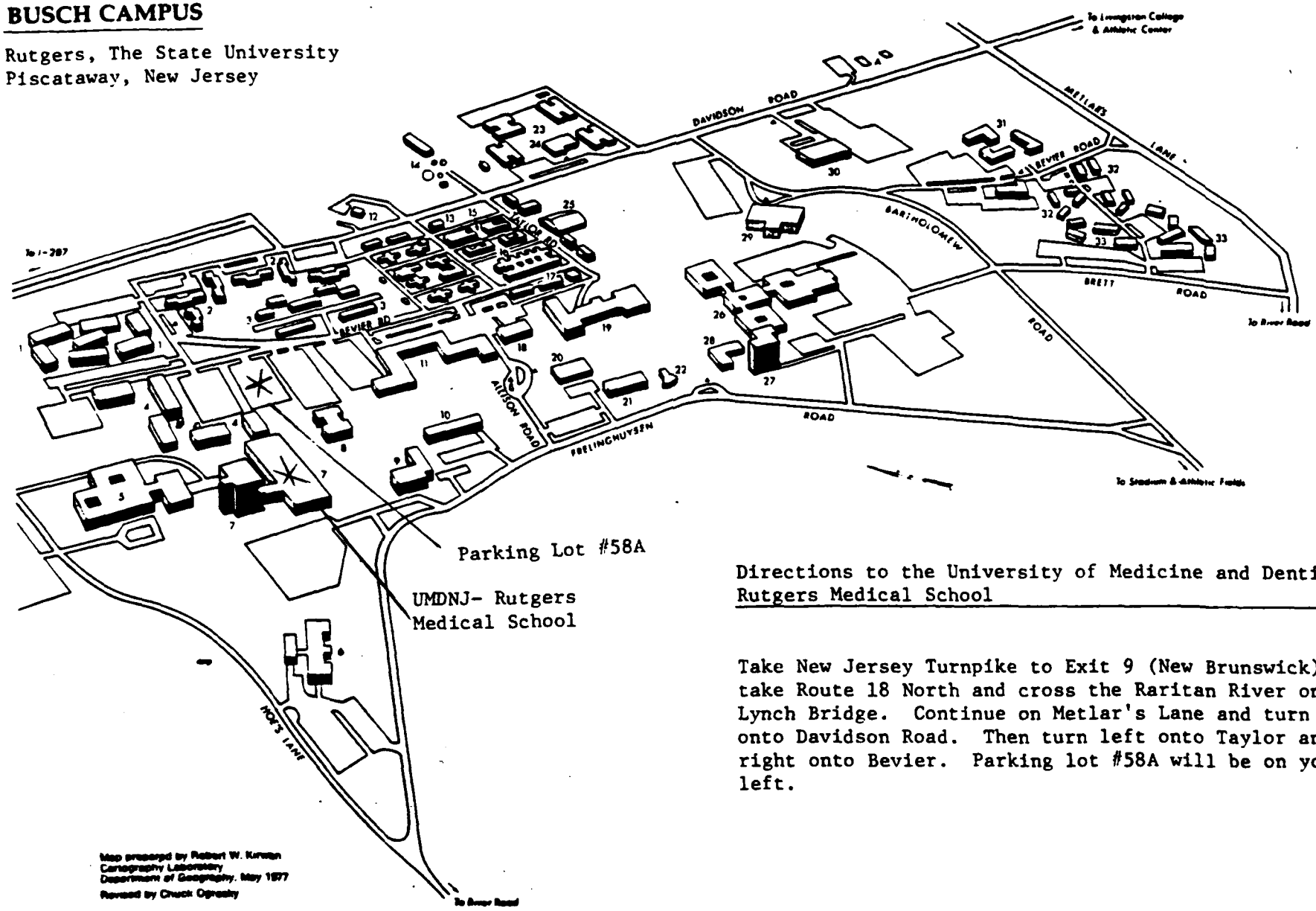
Piscataway, New Jersey



Directions to the University of Medicine and Dentistry - Rutgers Medical School

Take New Jersey Turnpike to Exit 9 (New Brunswick)... take Route 18 North and cross the Raritan River on the Lynch Bridge. Continue on Metlar's Lane and turn left onto Davidson Road. Then turn left onto Taylor and right onto Bevier. Parking lot #58A will be on your left.

INFORMATION FOR AUTHORS

The preceedings of the Colloquium will be published next year under the title "Molecular Theories of Cell Life and Death". The deadline for the submission of manuscripts is September 1, 1986. All invited speakers are expected to submit a manuscript, 20-25 pages long typed in double space. In addition to the invited speakers, others attending the Colloquium are encouraged to submit a short communication (10-15 pages long typed in double space) that can contribute to the development of the main theme of the Colloquium. Before initiating writing, such persons are asked to contact in person or in writing any one of the members of the organizing committee (see p. 1 for address).

Style of Manuscript

General Instructions: 1) Manuscripts must be type-written, double-spaced with wide margins on 8.5- x 11-inch bond paper. Two copies should be submitted - the original and one clear photocopy. Two sets of illustrations must be submitted. 2) Pages should be numbered in the upper right-hand corner (beginning with the first text page). They should be arranged in the following order: title page, abstract and index terms, text, text footnotes, acknowledgments, references, tables, figure legends, illustrations. 3) The title page should have the title of the article; author(s); department and institution in which the work was done with city, state and zip code, or country; an abbreviated title for the running head (not exceeding 55 characters including spaces between words); name and address for mailing proofs. 4) The abstract and index terms should be on a separate sheet, all lines double-spaced. 5) Text footnotes, acknowledgments, references, and figure legends should begin on separate sheets, all lines double-spaced. 6) Each table should be typed on a separate sheet and double-spaced. 7) Illustrations should be identified on the reverse (lightly with a soft pencil) with figure number and name of first author; when necessary, the top should be marked. 8) The text should be clear and concise, conforming to accepted standards of English style and usage. Unfamiliar or new terms should be defined when first used.

Title: The title, a widely circulated part of the article, should be informative. It should contain no unnecessary words like "Studies in ....." and should not exceed 85 characters, including spaces between words.

Abstract: A one-paragraph informative abstract of not more than 170 words must accompany each manuscript.

Index Terms: A list of three or more words or short phrases not included in the title should be appended to the abstract.

Abbreviations, Symbols, and Terminology: Include in the manuscript a list of new or special abbreviations used in the paper, with spelled-out form or definition if necessary. For commonly accepted abbreviations, word usage, symbols, etc., authors are referred to the CBE Style Manual (3rd ed., AIBS, 1972). Chemical and biochemical terms and abbreviations should be in accordance with the recommendations of the IUPAC-IUB Combined Commission on Biochemical Nomenclature.

Footnotes: Text footnotes should be numbered consecutively throughout. They should be double-spaced and assembled on one sheet.

References: References should be typed separately, double-spaced (**do not single space any line**), arranged alphabetically by author. In the text, references should be included in parentheses (last names of no more than first two authors followed by the year of publication; in case of more than three authors, last name of only first author followed by et al.). The style of citation should be as follows:

Journal Articles. Last name of first author, followed by initials; initials and last names of each coauthor; title of article (first word only capitalized); name of journal (abbreviated as in Chemical Abstracts List of Periodicals); volume, inclusive pages, and year. Example: 1. Chisholm, D.J., J.D. Young, and L. Lazarus. The gastrointestinal stimulus to insulin release. J. Clin. Invest. 48:1453-1460, 1969.

Book References: Author(s) as above; title of book (main words capitalized); city of publication; publisher; year and pages.

Illustrations: Two complete sets of figures are required. Figures should be sharp, unmounted glossy photographic prints not larger that 8.5 x 11 inches. Do not submit original drawings. Each must be identified. Particular attention should be given to the following:

1) Illustrations should be numbered consecutively with arabic numerals and referred to as figures.

2) Figures should be prepared for single-column width (3.5 inches), whenever possible; otherwise, for double-column width (7 inches).

3) Actual magnification of photomicrographs should be given. **A length scale on the print is preferable.**

4) Special features on photomicrographs should be designated by letters, figures, and arrows that contrast with the background.

5) Lettering should be done in india ink by a draftsman. It must be proportionate to the size of the illustration if it is to be legible after reduction. It should be sized so that its smallest elements will be not less than 2 mm high after reduction.

6) Photographs of equipment should be used sparingly; good line drawings are usually more informative.

7) Figures in color are accepted if the author can assume all printing costs. Two positive color prints should be supplied.

8) The approximate position of each figure should be indicated in the margin of the manuscript.

9) Each figure must have a legend. Legends should be grouped in numerical order and typed double-spaced on one or more sheets.

Tables:

1) Tables should be numbered consecutively with arabic numerals.

2) Each table should be typed double-spaced on a separate sheet.

3) Each table should have a brief title; explanatory matter should be in footnotes, **not in the title.**

4) Tables must not duplicate material in text or illustrations.

5) Nonsignificant decimal places in tabular data should be omitted.

6) Short or abbreviated column heads should be used and explained if necessary in footnotes.

7) Statistical measures of variations, SD, SE, etc., should be identified.

8) Table footnotes should be listed in order of their appearance and identified by standard symbols * † ‡ § for four or fewer; for five or more, consecutive superior letters should be used throughout.

9) The approximate position of each table should be indicated in the margin of the manuscript.

Mathematical Formulas and Equations:

Presentation of mathematical aspects of articles should be addressed to the many readers of the publication who are not mathematicians. There should be a statement of the mathematical strategy and a summary of the meaning of the final mathematical statement, the assumptions and limitations.

Structural chemical formulas and complicated mathematical equations should be simplified as much as possible and carefully checked. All subscripts, superscripts, Greek letters, and other unusual characters must be clearly identified in pencilled marginal notes where they first appear. Distinguish between 1 (one) and the letter l (el), zero and the letter O, x (mathematical sign) and the letter x. Use the slant line (/) for simple fractions (a + b)/(x + y) rather than the built-up fraction $\frac{a+b}{x+y}$, which requires an additional line of space.

(Submitted to Academic Press)

APPENDIX III

S. Ji, R. Snyder, R. Trelstad, S. Finette and M. W. Anders, eds.

MOLECULAR THEORIES OF CELL LIFE AND DEATH

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thermal cycle secondary to the rotation of the earth around the sun. These frustrations of Anderson are theoretically related to the concept of conformons (conformational strains of biopolymers carrying free energy and genetic information) proposed in 1972 independently by Green and Ji and by M. V. Volkenstein.

#4. D. Kondepudi, Department of Physics, University of Texas, Austin, Texas.

"Origin of Biomolecular Chirality"

Of the two (L & D) optical isomers possible for each amino acids, the L isomers are utilized almost exclusively by living systems. This mysterious phenomenon has not yet been satisfactorily explained. In this article, Dr. Kondepudi presents a theoretical model of the chiral symmetry breaking that is based on the notion that small energy difference between the L and D isomers due to weak neutral current interactions ($\Delta E/kt = 10^{-17} - 10^{-15}$) can give rise to a chiral selection under far-from equilibrium conditions of Prigogine.

@5. B. Hess and M. Markus, Max Planck Institute for Nutrition Physiology, Dortmund, West Germany.

"Dissipative Structures in Biochemical Systems"

The first concrete experimental support for the concept of dissipative structures is provided in chemistry by the Belousov-Zhabotinsky reaction discovered in 1958. Subsequent investigations in Hess' Institute in Dortmund have now clearly demonstrated that dissipative structures of Prigogine can exist in biochemical systems such as cell-free extracts of glycolytic enzymes and isolated mitochondria. The relevant experimental data and theoretical interpretations are reviewed and their possible implications in cell biology emphasized.

#6. K. Porter, Department of Biological Sciences, University of Maryland, Catonsville, Maryland.

"Evidence for the Organization of the Cytomatrix"

Dr. Porter is one of the codiscoverers of the cytoskeletal system in the living cell. He reviews the old and the new experimental evidence indicating the elaborate spatio-temporal organization of cytomatrix materials and discusses their possible roles in cellular functions.

#7. G. R. Welch, Department of Biological Science, University of New Orleans, New Orleans, Louisiana.

"Cytosociology and the Metabolic Space-Time"

Classical biochemistry developed through studies on enzymes solubized in homogeneous aqueous media. But, as Porter's Chapter clearly demonstrates, the biochemistry that goes on inside the living cell may be highly organized in space and time. Dr. Welch develops a

general theoretical framework applicable to enzyme behaviors in the zero (i.e., in homogeneous solution), one (e.g., in substrate channeling with or without microtubules), two (e.g., membranous enzymes), three (in anisotropic volume such as the cytomatrix), and four dimensions (e.g., spatio-temporal evolution of chemical concentration gradients inside the cell such as myocytes and neutrophils). The relationship between the concept of cytosociology and the dissipative structure theory of Prigogine on the one hand and that between cytosociology and intracellular dissipative structures essential in the model of the living cell proposed by S. Ji on the other are pointed out.

*8. M. Holcombe, Department of Computer Science, University of Sheffield, Sheffield, England.

"Toward a Formal Description of Intracellular Biochemical Organization" (25 pages)

The theoretical framework that is rapidly emerging as a result of the discovery that the cytomatrix is exquisitely organized in space and time are difficult to be accurately expressed using the traditional concepts and terminologies inherited from "soluble" enzymology and biochemistry. To circumvent these difficulties, Dr. Holcombe has begun to apply the algebraic language developed by mathematicians to describe man-made machines including computers to the description of complex biochemical networks in cells. His investigations have highlighted the similarities as well as the differences between man-made machines and Nature-made machines such as the living cell.

*9. A. Scott, Department of Electrical Engineering, College of Engineering, University of Arizona, Tuscon, Arizona.

"Solitons as Free Energy Carriers in Biopolymers" (23 pages)

Solitons are solitary wave packets that can propagate through condensed media such as water, glass, and biopolymers without significant dissipation of energy. This unique property arises from the non-linearity of the equations of motion involved. The concept of solitons as a means to transfer free energy in biopolymers was first suggested by A. Davydov in 1973 and has been subsequently validated by computer simulations in Scott's laboratory. Recent developments in soliton physics are reviewed and their potential applications to enzymology and DNA transcription and replication mechanisms discussed. In a certain sense, solitons are indistinguishable from the concept of conformons defined by Green and Ji in 1972; in another sense, solitons can be viewed as evolutionary precursors of conformons.

#10. J. Rothstein, Department of Computer and Information Science, Ohio Sate University, Columbus, Ohio.

"Non-Dichotomous, Relative and Hierarchical Aspects of Life and Death"

Modern information theorists have extended the concept of information first mathematically defined by Shannon in 1948 to include not only

linear sequences of symbols but also two or three dimensional structures. In this article, Dr. Rothstein attempts to increase the dimensionality of information further by including the phenomena of dynamic organization of various physical and chemical processes in space and time, leading to an information-theoretic definition of life and death on the cellular and multicellular levels.

*11. S. Orrenius, Department of Toxicology, Karolinska Institute, Stockholm, Sweden.

"Molecular Mechanisms of Cell Death" (23 pages)

The cell injuries caused by the analgesic, acetaminophen, has been intensely investigated during the past 15 years and provide perhaps the best studied experimental system in molecular toxicology. Dr. Orrenius summarizes most recent results in this area and proposes a molecular model of acetaminophen-induced liver cell death which may apply generally to other chemically induced cell injuries and necrosis.

*12. H. Sies, Institute of Physiological Chemistry, University of Düsseldorf, Düsseldorf, West Germany.

"Electronically Excited States in Cells and Organs: Relation to Prooxidant/Antioxidant Balance" (26 pages)

Dr. Sies and his collaborators have developed experimental techniques for continuously monitoring weak light emissions from intact cells and perfused organs. These light emissions result from the transitions of electronically excited oxygen atoms to their ground states. They have opened up a new frontier in biological research involving electronically excited states of biomolecules in cell life and death. The experimental methodology and recent results of the "excited-state biochemistry" are presented and their possible roles in physiology and pathophysiology are discussed.

*13. H. de Groot and T. Noll, Institute for Physiological Chemistry, University of Düsseldorf, Düsseldorf, West Germany.

"Hypoxia and Molecular Mechanisms of Cell Death" (40 pages)

These authors have recently obtained experimental evidence that oxygen may have dual effects on cellular functions - under normal oxygenation conditions (normoxia) oxygen is predominately beneficial to cells; however, under suboptimal oxygenation conditions (hypoxia) oxygen not only contributes to cell life but also participates in perpetuating cell damaging processes through its ability to promote radical chain-propagation reactions such as in lipid peroxidation. Based on these results, de Groot and Noll propose a novel mechanism of cytotoxicity of activated oxygen species which may have potentially important applications in developing rational therapeutic strategies for circulatory diseases in man.

#14. M. W. Anders, Department of Pharmacology, University of Rochester School of Medicine and Dentistry, Rochester, New York.

"The Role of Covalent Binding in Chemical Cytotoxicity"

The discovery in 1973 by Mitchell, Jollow, Gillete et al. that the acetaminophen-induced liver injury was associated with metabolic activation of the drug into reactive intermediates which bound covalently to cellular constituents was a major breakthrough in the history of toxicology. Experimental developments since then have now established the notion that, although covalent bindings are necessary for some cytotoxic mechanisms, the binding of reactive intermediates of cytotoxicants alone is often not sufficient to cause cell injuries and death. In preparation for a new global mechanism of chemical cell injury, the current developments in metabolic activation of cytotoxic chemicals are reviewed and their significance highlighted.

15. R. Trelstad, Department of Pathology, the University of Medicine and Dentistry of New Jersey Robert Wood Johnson School of Medicine, Piscataway, New Jersey.

"Productive Cell Death"

There are many examples in biology where the survival of an organism depends critically on programmed deaths of a certain subset of the cells constituting the organism (e.g., the death of the müllerian duct cells in developing human embryos in order for the wolffian duct cells to form male sex organs; the phenomenon of "apoptosis" wherein certain cells are programmed to die upon receiving appropriate signals). Thus, death on one level of the biological hierarchy is essential for life on another level, and vice versa. Possible roles of such programmed cell deaths in health and diseases are reviewed.

* 16. J. R. Hiernaux, P. Meyers and R. Lefever, Department of Physical Chemistry, Free University of Brussels, Brussels, Belgium.

"Population Dynamics of Tumors Attacked by Immunocompetent Killer Cells" (23 pages)

Certain dynamical aspects of the interactions between tumor cells and cytolytic cells of the immune system of the host can be quantitatively studied using the mathematical formalisms of population dynamics. Such mathematical formalisms are summarized in this article, and some testable predictions are formulated on the basis of a kinetic model of tumor cell-immunocompetent killer cell interactions.

17. H. Westerhoff and J. G. Koster, Laboratory of Molecular Biology, National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases, National Institute of Health, Bethesda, Maryland.

"The Regulation and Control of Histone Gene Expression in Early Developments"

A kinetic model of the histone gene expression in developing Xenopus has been formulated on the basis of the existing experimental data. The model suggests that a significant fraction of the genetic information in developing Xenopus is transferred from parent to

daughter cells via a non-nuclear, m-RNA-mediated mechanism.

#18. S. Finette, Department of Biomedical Engineering, College of Engineering, Rutgers University, Piscataway, New Jersey.

"Emergent Properties, Reliability and Holistic Death in Neural Network"

Using computer simulations it is demonstrated how a network of several hundred neurons can exhibit new properties not possessed by individual neurons. Possible implications of such emergent properties of cellular networks are discussed in relation to the mechanisms of brain functions and malfunctions.

@19. S. Ji,[1] Z. Y. Zhang[2] and Y. M. Han[3], [1]Department of Pharmacology and Toxicology, College of Pharmacy, [2]Department of Physics, Rutgers University, Piscataway, New Jersey, and [3]Department of Physics, Duke University, Durham, North Carolina.

"Application of Local Gauge Field Theories to Biopolymers"

To describe history-dependent properties of non-living systems (e.g., atomic nuclei, the Big Bang), physicists utilize local gauge field theories developed since the 1950's. The same local gauge field theories may be useful in describing the unique catalytic properties of enzymes which have been elaborated by past evolution. The article explores the possibility of viewing the functional consequences of the genetic information associated with the linear sequence of amino acids in enzymes as an example of local gauge fields. It is pointed out that, if local gauge fields are proven to exist in informational biopolymers, the existence of a new force in enzymes will have been demonstrated and a new unity between biology and physics will have been revealed.

*20. R. A. Neal, Chemical Industry Institute of Toxicology, Research Triangle Park, North Carolina.

"How Fundamental Knowledge Can Help Solve Practical Problems in Toxicology" (18 pages)

Toxicology is one of the newest and most rapidly expanding branches of life sciences today. Like in any such active fields, toxicologists often find it difficult to agree on what toxicology is and what it is not. Dr. Neal summarizes the most widely accepted view of what the discipline of modern toxicology is and should be. In addition, he succinctly points out how the basic scientific knowledge about life and death on the molecular level would help toxicologists to accomplish one of their major missions, namely predicting the toxicity or lack of toxicity of chemicals to humans.

#21. S. Ji, Department of Pharmacology and Toxicology, College of Pharmacy, Rutgers University, Piscataway, New Jersey.

"Biology and Beyond" (40 pages)

There is a revolution now waging in physics with the advent of the superstring theory that has the capacity to unify all the four forces in Nature; similarly, the developments in molecular biology that have occurred during the past 2-3 decades have provided an evidence to support the view that an equally fundamental but silent revolution may be in progress in biology. This view is based on the following considerations: (1) The fundamental unit of all living systems is the cell, and hence all experimentally observable properties of living systems reflect some aspects of the cell; (2) the ultimate solutions to all major biological problems such as chemical toxicity, cancer, morphogenesis, and brain functions may not emerge independently and separately but overlap with one another in the sense that the solution in one field may provide solutions to all other fields as well; and finally (3) it is possible to formulate a theoretical model of the living cell utilizing only those concepts and ideas that are rooted in experimental science - namely, the Watson-Crick mechanism of genetic inheritance, the conformon theory of enzymic catalysis, and the dissipative structures of Prigogine.

The theoretical foundations underlying the physics revolution is superstrings and that responsible for the biological revolution can be ascribed to conformons. What is unexpected is the possibility that these two fundamental entities may share common properties - i.e., superstrings and conformons may be symmetric with respect to their possessing both energy and information. The higher dimensional entity containing both energy and information was termed "gnergy" in 1985, and this may provide the ultimate symmetry capable of unifying physics and biology on the one hand and life and non-life on the other.

*Manuscripts received as of April 22, 1987 (8)

#Manuscripts in preparation for submission by July 31, 1987 (10)

@Manuscripts under negotiation (3)

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